

Dementia with Lewy bodies – a case report, diagnosis and management

Otępienie z ciałami Lewy-ego – opis przypadku klinicznego, diagnoza i leczenie

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KEYWORDS:

- dementia with Lewy bodies
- clinical symptoms
- neuroimaging
- diagnostic difficulties
- treatment

ABSTRACT

Dementia is one of the major health issues around the globe which can severely affect the daily functioning of patients and their caregivers. There is no pharmacological method that entirely cures dementia, however, early detection, precognitive medication and treatment of concomitant illnesses and behavioural symptoms can significantly moderate cognitive decline as well as improve the quality of life patients with dementia. Here we present a case of Dementia with Lewy Bodies (DLB), which is the second most common form of neurodegenerative dementia in population above 65 years old. Despite its common occurrence, this disease is rarely detected, due to misleading symptoms, in its early stage. DLB often starts with depressive or psychotic symptoms, whilst cognitive decline is not apparent yet. Clinical features of DLB, as well as challenges of diagnosis and management are presented accordingly.

SŁOWA KLUCZOWE:

- otępienie z ciałami Lewy'ego
- objawy kliniczne
- neuroobrazowanie
- trudności diagnostyczne
- leczenie

STRESZCZENIE

Otępienie jest jednym z głównych problemów zdrowotnych na całym świecie, który ma wpływ na codzienne funkcjonowanie pacjentów i ich opiekunów. Nie istnieje żadna metoda farmakologiczna, która w pełni wyleczy demencję jednak wczesne wykrycie, zastosowanie leków prokognitywnych oraz leczenie współistniejących chorób i objawów behawioralnych, może znacząco poprawić jakość życia pacjentów z otępieniem. W pracy przedstawiono przypadek otępienia z ciałami Lewy'ego (DLB), który pod względem częstości występowania jest drugim pierwotnie zwyrodnieniowym zespołem otępiennym w populacji powyżej 65 roku życia. Pomimo częstego występowania, ta choroba jest rzadko wykrywana ze względu na mylące objawy we wczesnym stadium. DLB często zaczyna się od objawów depresyjnych lub psychiatrycznych, podczas gdy obniżenie funkcjonowania poznawczego nie jest jeszcze widoczne. Kliniczne cechy DLB, jak również wyzwania związane z diagnostyką i leczeniem, przedstawiono poniżej.

Introduction

According to the current estimates of World Health Organization (WHO) around 50 million people globally have dementia, and nearly 10 million new cases of dementia are diagnosed every year. Dementia with Lewy bodies (DLB) is the second most common cause of primary neurodegenerative dementia and is responsible for 10-20% of all cases of dementia (1). DLB is characterized by aggregation of the protein alpha-synuclein in the brainstem, limbic and neocortical regions (2). These pathological concentrations of protein have an impact on patient's behaviour, cognition, motor and autonomic functions (3).

The diagnosis of DLB is based on criteria developed by an international collaboration of experts – the Dementia

with Lewy Bodies Consortium (DLB Consortium). The first recommendations were published in 1996, and throughout years criteria were modified to increase the sensitivity in detection of DLB. The newest criteria published in 2017 distinguish between clinical features and diagnostic biomarkers. Clinical symptoms are divided into core and supportive clinical features, correspondingly biomarkers are divided into indicative and supportive features (see Table 1). The existence of at least two core clinical features, or one core clinical feature with one or more indicative biomarkers is necessary to diagnose a probable DLB (4).

DLB is a progressive disease, which is characterized by a variety of cognitive, psychotic, neurological, mood, motor and autonomic symptom. The course of disease differs in particular patients. One of the reasons why DLB is rarely

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Table 1. Clinical features and biomarkers used for the diagnosis of Dementia with Lewy Bodies (4).

Core clinical features:	Indicative biomarkers:
<ul style="list-style-type: none"> fluctuating cognition; recurrent visual hallucinations; parkinsonism (bradykinesia, rest tremor or rigidity); REM sleep behaviour disorder (RBD). 	<ul style="list-style-type: none"> reduced dopamine transporter uptake in basal ganglia demonstrated by PET/SPECT; abnormal uptake ¹²³I-iodine-MIBG in scintigraphy of myocardium; REM sleep without atonia confirmed in polysomnography (RWA).
Supportive clinical features:	Supportive biomarkers:
<ul style="list-style-type: none"> sensitivity to antipsychotic medication; postural instability; falls; syncope; autonomic dysfunction (e.g., urinary incontinence, constipation, or orthostatic hypotension); hypersomnia; hyposmia, hallucinations different from visual; systematized delusions; apathy, anxiety, and depression. 	<ul style="list-style-type: none"> relative preservation of medial temporal lobe on CT/MRI; low-uptake on SPECT/PET perfusion scan with reduced occipital activity +/- the cingulate island sign on FDG-PET imaging; prominent posterior slow wave activity on EEG with periodic fluctuations in the pre-alpha/theta range.

diagnosed, is that that in the early stage of DLB, diminished cognitive functioning is not apparent. Psychotic symptoms which occur in older people can be mistaken as psychosis, delirium and are treated with antipsychotic medication, what can cause extrapyramidal symptoms in DLB patients. There is not known any treatment which can cure this disease, but pharmacological and non-pharmacological methods can improve the patient's quality of life. The diagnosis and management symptoms of DLB symptoms requires cooperation of clinicians many specialities (3, 5).

The purpose of this article is to summarize the diagnostic criteria, clinical features and management of DLB in order to draw attention of clinicians who are taking care of patients with a suspected case of dementia. We have reviewed current guidelines on diagnosis and treatment of DLB. This case report illustrates the importance of clinical course of disease, when the highly specific biomarkers such as PET/SPECT, MIBG myocardial scintigraphy, and polysomnography are not possible to use. Data presented below was anonymised.

Case report

A 64-year old woman was referred to psychiatric department with the following symptoms: deterioration in general functioning, sluggishness, apathy, and depressed mood. Three years before, patient's family noticed subtle changes in patient's behaviour: difficulties with decision making, decreased activity, avoidance of social meetings. Five months before admission to the clinic, patient complained of memory problems, which caused difficulties at work, and recurrent visual and auditory hallucinations. The patient was examined by a psychiatrist in the outpatient clinic and was prescribed 20 mg of citalopram and 50 mg of perazine per day. As a result of implemented treatment, a slight improvement was observed – hallucinations disappeared but at the same time bradykinesia, generalized fatigue, difficulties with initiation of movements, shuffling gait appeared.

In the hospital, the patient complained of depressed mood, lower activity, impairment of short-term memory and concentration. She described her previously experienced

visual and auditory hallucinations as pleasant – she was observing non-moving human figures behind her window, and was hearing the sound of opening doors or windows.

The neurological examination revealed the symptoms of Parkinson syndrome, such as monotonous, blurred speech, disturbances in speech prosody, hypomimia, bradykinesia, postural instability, forward-flexed posture. In the examination of extremities there was an increased muscle tone, deterioration in precise movements of the hands and apraxia. The patient also complained of recurrent falls, syncope, and urinary incontinence. The computer tomography and magnetic resonance imaging showed temporal atrophy bilaterally.

Neuropsychological evaluation including: Mini-Mental State Examination (MMSE), the Clock Drawing Test (CDT), Benton Visual Retention Test (BVRT), Color Trails Test (CTT), California Verbal Learning Test (CVLT), the Wechsler Adult Intelligence Test-Revised [WAIS-R (PL)], Verbal Fluency Test (VFS) revealed severe deficits in cognition functioning, especially in visuospatial functioning, attention maintaining, visuo-motor coordination, learning, short-and long term memory. The MMSE result was confined with mild degree dementia.

The diagnosis was confirmed by the presence of three out of four core clinical features: worsened cognition, recurrent visual hallucinations and bradykinesia. The diagnosis of DLB was also supported by sensitivity to antidopaminergic treatment, urinary incontinence, apathy, and anxiety.

During hospitalization the patient was treated with levodopa/benserazide 62,5 mg four times per day, levodopa/benserazide modified release capsule once daily and rivastigmine 1,5 mg twice daily. After three weeks of such medication, significant changes in motor function (reduction in slow motion, improvement of precise movements and walking) and marked improvement in cognition, general activity, and mood were observed.

Discussion

The patient was initially hospitalized as a case of depression with apathy and psychomotor retardation, with

a history of brief visual and auditory hallucinations. Due to information provided by patient's family about observed cognitive and general functioning decline, a possible case of dementia was suspected, and further diagnostic tools were performed.

In this case report, within five months from appearance of cognitive impairment, apathy and hallucinations, the extrapyramidal symptoms occurred after the treatment with perazine, and persisted after discontinuation of antipsychotic drug. According to the newest diagnostic criteria of DLB defined by DLB Consortium, repeated complex visual hallucinations can appear in even 80% patients with DLB, and parkinsonism can occur up to 85% cases, and is expressed by one of these features: bradykinesia, tremor, or rigidity. If the motor symptoms occur before dementia by at least 1 year, dementia in Parkinson's disease (PDD) should be diagnosed (4).

Relative preservation of medial temporal lobe structures is a supportive biomarker for criteria of DLB. In this case, the medial temporal atrophy (MTA) was visible in the MRI, what does not support the diagnosis of DLB, but is an indicator for Alzheimer's disease (AD). However, recent studies showed that more than 50% of patients diagnosed with DLB have brain lesions like in AD-MTA or dorsal midbrain atrophy, so it is challenging to distinguish DLB patients from AD patients based only on MRI (6). The hippocampal-sparing is the most prevalent pattern in DLB patients, and is specified by lack of MTA with atrophy of the posterior and/or frontal cortex (7).

The newest guidelines of DLB diagnosis insist on the use of biomarkers such as dopamine transport imaging in PET/SPECT, MIBG myocardial scintigraphy, and polysomnography. Those biomarkers together have a high specificity (4). Unfortunately, those methods are not often available and routinely performed in many clinics. In most of Polish hospitals the diagnosis of DLB is based on the clinical course of the disease, response to the implemented treatment, and is supported by neuroimaging methods such as MRI or CT.

Compared to AD, DLB is related with worse prognosis, in particular: faster worsening of cognitive functions, shorter life expectancy and higher probability of a need of placement in the nursing house (3). The management of patients with DLB needs a complex approach including pharmacotherapy of cognitive, psychiatric and motor syndromes, and as well a support of caregivers (4). There are no known disease-modifying therapies for DLB. Recent research focuses on drugs that decrease alpha-synuclein production and aggregation (8). Based on data from systematic reviews and meta-analyses, cholinesterase inhibitors – donepezil and rivastigmine were equivalently effective in improving cognitive and neuropsychiatric symptoms and daily functioning in patients with DLB (5).

Almost 85% of patients with DLB suffer from parkinsonian features which tend to be less sensible to levodopa therapy, and there is a higher risk of treatment-emergent psychotic symptoms which actually was not the case in our patient. Levodopa can be used in patients with motor symptoms, but it should be started at low dose and gradually increased (4, 5).

Olfactory dysfunction (anosmia, hyposmia), reduced bowel peristalsis, depression can precede the onset of memory problems in DLB. Individuals who suffered from those symptoms, had reduced cardiac MIBG uptake, which can be a promising factor of diagnosing prodromal state (9). In another study it was found that women presented with

different symptoms than men before establishing the diagnosis of DLB. More women experienced psychiatric syndromes (such as visual and auditory hallucinations, delusions, depression), whilst man presented more commonly with RBD, parkinsonism, hyposmia, and syncope (1).

The presented case illustrates diagnostic process of DLB. It included psychiatric and neurological examination, neuropsychological evaluation and neuroimaging. The diagnosis of DLB was also supported by the clinical course of disease, and reaction to the treatment. Post-mortem studies showed that DLB was detected in 22,5% of general, population and 41,4% of the demented, often occur with AD (8). The detectability of DLB is much lower than expected.

Clinicians often do not take into consideration the diagnosis of probable DLB in the group of elderly patients who are complaining of memory problems and decline during daily functioning. Core clinical symptoms of DLB are often misinterpreted such as fluctuating cognition is mistaken as AD or vascular dementia, parkinsonian features as PD, hallucinations as psychosis or delirium. Current guidelines put an impact on biomarkers such as PET/SPECT, myocardial scintigraphy, polysomnography, but they are not routinely performed. Careful anamnesis and extensive neuropsychological assessment are still the most valuable tools in most hospitals. Treatment of DLB is complex and it includes management of cognitive, neuropsychiatric, autonomic and motor symptoms. Acetylcholinesterase inhibitors such as donepezil or rivastigmine are efficient in cognitive and neuropsychiatric symptoms: apathy, fear, delusions, hallucinations. Levodopa has been shown as beneficial in motor symptoms, but should be gradually increased cause it can evoke hallucinations.

The diagnosis of DLB is challenging for psychiatrists and neurologists who are mainly dealing with patients suffering from dementia. The greater availability of PET/SPECT, myocardial scintigraphy and polysomnography can improve diagnostic accuracy in distinguishing DLB and AD and give information about coexisting AD pathology in DLB (4). There is a need to create guidelines of diagnosing prodromal stages of DLB, and use of new biomarkers such as α -synuclein imaging, or biopsies of skin and other tissues which can reveal the alpha-synuclein deposits (8).

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